Unveiling Garlic's Arsenal: A Comprehensive Review of Antifungal and Antibacterial Cream

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ABSTRACT
Garlic (Allium sativum) has long been recognized for its medicinal properties, particularly its antimicrobial effects. In this comprehensive review, we explore the therapeutic potential of garlic in the formulation of creams targeting fungal and bacterial infections. We discuss the rising prevalence of fungal infections, particularly those caused by Candida species, and the challenges they pose in healthcare settings. Furthermore, we delve into the diverse biochemical composition of garlic, including sulfur compounds, enzymes, carbohydrates, minerals, amino acids, flavonoids, and vitamins, which contribute to its antimicrobial activity. The synthesis of allicin, a key bioactive compound in garlic, and its mechanism of action against various pathogens are elucidated. Additionally, we examine the dermatological applications of topical garlic in treating fungal skin infections, wound healing, antioxidant protection, UVB shielding, and anti-aging benefits. Clinical evidence supporting the efficacy of garlic extracts in managing viral skin conditions is also discussed. Finally, we highlight the need for further research and clinical trials to fully explore garlic's therapeutic potential, safety profile, and optimal formulations, thereby enhancing patient outcomes in the management of infectious diseases.

Keywords: Garlic, Antifungal, Antibacterial, Cream Formulation, Dermatological Applications, Antioxidant, Antiviral, Wound Healing.

Introduction
Over the past two decades, there has been a rise in the prevalence of fungal infections, marking them as emerging conditions within hospital environment. Analyzing the epidemiological data from various healthcare settings worldwide to identify key factors contributing to the prevalence and incidence of hospital-acquired infections (hais). They highlight the changing landscape of immunosuppressive illnesses, advances in medical technology, and evolving antimicrobial resistance patterns as significant drivers of hais[1]

Fungal disease This is increasing in very high ratio due to certain reason including opportunistic infection. Fungal infection caused by Candida has become more prevalent than Escherichia coli and Pseudomonas sp., Asprgellosis sp. and other sp.[2,3]
Candida albicans is the most common species in the genus which has been implicated in Candidiasis. Candidiasis, characterized as an opportunistic fungal infection caused by Candida species, manifests in diverse anatomical sites such as the oral cavity, vagina, penis, and other mucocutaneous regions. Without appropriate treatment, Candida infections can progress to systemic involvement, posing a heightened risk of sepsis and multi-organ dysfunction. Notably, within the oral cavity, Candida species exhibit varied morphologies, with common strains including C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. pseudotropicalis, C. stellatoidea, and C. tropicalis, each presenting unique challenges in diagnosis and management.

1. **Mucocutaneous Candidiasis**: This type involves infections of the mucous membranes and skin, such as oral thrush and genital candidiasis.

2. **Invasive Candidiasis**: This refers to systemic infections where Candida species invade the bloodstream and other organs, potentially leading to severe complications like sepsis.

3. **Esophageal Candidiasis**: Specifically mentioned as a subtype of candidiasis affecting the esophagus, causing symptoms like difficulty swallowing and pain behind the breastbone.

4. **Chronic Mucocutaneous Candidiasis (CMC)**: This type involves recurrent or persistent candidiasis of the skin, nails, and mucous membranes, often associated with underlying immune system disorders.[4]

![Figure. 1 C. albicans](image)

The purpose of the current study is also based on the medicinal property of a plant i.e. Garlic (Allium sativum) Garlic oil shows a wide range antimicrobial activity. Garlic (Allium sativum L.), a member of the Alliaceae family, holds a prominent place among essential vegetables globally. Its significance stems not only from its culinary applications but also from its therapeutic and medicinal properties, valued in both traditional and modern medicine. Every part of the plant, from the inflorescence to the leaves and cloves, has been utilized since ancient times as a condiment or spice, enhancing the flavor of soups, sausages, and salads.[5]
Types of Garlic(6)
There are different types of garlic with their specific feature:

- **Softneck garlic**: Often found in markets, this is the most common type of garlic with soft skin and creamy white colour.
- **Silver garlic**: It has a pink tint on its outer covering and has a very pungent aroma.
- **Artichoke garlic**: It has a mild flavour with large and fewer cloves
- **Hardneck garlic**: It has a hard, woody stalk with a purple colour of the outer skin.

Geographical source: Central Asia, Southern Europe, USA, India

The biochemical constituents of garlic bulb:

1. **Sulfur Compounds**: Allicin, alliin, S-allylcysteine (SAC), S-allylmercaptocysteine (SAMC), diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), and ajoene.
2. **Enzymes**: Allinase, peroxidase, and miracynase.
3. **Carbohydrates**: Sucrose and glucose.
4. **Minerals**: Selenium, germanium, calcium, copper, iron, potassium, magnesium, and zinc.
5. **Amino Acids**: Lysine, histidine, arginine, aspartic acid, threonine, serine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, and phenylalanine.
6. **Flavonoid Compounds**: Apigenin, quercetin, nobiletin, tangeretin, rutin, allixin, myricetin, bergamottin, cyanidin, allistatin I, and allistatin II.
7. **Sapogenins and Saponins**: Various types have been identified, including proto-eruboside B, eruboside B, proto iso-eruboside B, isoeruboside B, sativoside B1, R1, R2, β-chlorogenin, and others. These have demonstrated cholesterol-lowering effects in animals and exhibit antifungal, antitumor, and cytotoxic activities.
9. **Other Constituents**: Water (65%), carbohydrate (28%), organosulfur compounds (2.3%), proteins (2%), free amino acids (1.2%, mainly arginine), fiber (1.5%), lipids (0.15%), phytic acid (0.08%), free radicals, and volatile oils.
These constituents collectively contribute to the various health benefits associated with garlic consumption, including its antioxidant, antimicrobial, anti-inflammatory, and cardiovascular effects.[7]

**Uses:**
- Antifungal
- Antibacterial
- Wound healing
- Antioxidant property
- Antiaging
- Viral infections
- Anti-diabetic

**Description**[8]

Garlic (*Allium sativum* L.) is a bulbous plant with distinct characteristics:

1. **Plant Structure**: It typically grows to about 60 cm in height.

2. **Bulb**: The bulb of garlic is rounded and consists of up to approximately 15 smaller bulblets, known as cloves. These cloves and the larger bulb are covered by a thin papery coat, which can be whitish or pinkish in color.

3. **Leaves**: Garlic plants have four to twelve long, sword-shaped leaves that are attached to an underground stem.

4. **Inflorescence**: The inflorescence of garlic is a spike that can grow up to 25 cm in length. Flower stalks arise from a common point. The flowers themselves are greenish white or pinkish and typically have six perianth segments (sepals and petals) measuring about 3 mm in length.

5. **Reproductive Characteristics**: Garlic flowers often abort before reaching full maturity, and thus, they usually do not develop into fruits. Seeds, if produced, are approximately half in size and have a black coat similar to onion seeds.

These features collectively define the appearance and structure of the garlic plant, distinguishing it from other members of the *Allium* genus.

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**Figure. 2 Synthesis of Allicin from alliin precursor**

The synthesis of allicin from its precursor alliin is a key biochemical process in garlic (*Allium sativum*). Allicin is a sulfur-containing compound responsible for many of garlic's medicinal properties, including its antimicrobial effects.
The process involves the enzymatic conversion of alliin to allicin through the action of the enzyme alliinase. When garlic is chopped, crushed, or otherwise damaged, alliinase comes into contact with alliin, leading to its conversion into allicin. This conversion occurs rapidly and is responsible for the characteristic pungent odor associated with fresh garlic. Allicin is highly unstable and quickly breaks down into various sulfur-containing compounds, which contribute to garlic's distinctive flavor and aroma. This synthesis process is central to understanding garlic's therapeutic properties and its traditional use as a natural remedy for various ailments, including fungal and bacterial infections.

Mechanism of action[17]
Allicin, with its short lifespan and high reactivity, poses a challenge for bacteria, viruses, and fungi due to its nonspecific action. In mammalian cells, allicin triggers cell death and proliferation while increasing plasma membrane permeability, hindering the growth of various bacteria and fungi and reducing biofilm formation. Its permeability through membranes is enhanced by interactions with thiols. This diverse mechanism of action suggests potential for sustainable drug design and may contribute to the emergence of multidrug-resistant bacterial strains. Allicin's antimicrobial activity affects both Gram-positive and Gram-negative bacteria and fungi, and combining it with other antimicrobials can enhance its effectiveness. Additionally, its volatile nature enables it to kill bacteria through the gas phase, with just one hour of exposure capable of halting microbial growth entirely.

Adverse reactions
Adverse reactions to garlic consumption or topical application can occur in some individuals, although they are relatively rare. These adverse reactions may include:

**Gastrointestinal Disturbances:** Garlic consumption, especially in large amounts, can cause gastrointestinal symptoms such as heartburn, bloating, gas, nausea, and diarrhea in some people.

**Skin Irritation:** Applying garlic or garlic extracts topically may lead to skin irritation, redness, itching, or dermatitis, particularly in individuals with sensitive skin or allergies to garlic. Potential

**Blood Thinning:** Garlic has blood-thinning properties, which can increase the risk of bleeding, especially when consumed in large amounts or in combination with blood-thinning medications. This can be a concern for individuals undergoing surgery or with bleeding disorders.

**Interaction with Medications:** Garlic supplements may interact with certain medications, including blood-thinning drugs, immune-suppressing medications, and some HIV/AIDS medications, affecting their efficacy or safety.

**Allergic Reactions:** While rare, some people may be allergic to garlic, experiencing symptoms such as hives, itching, swelling, or difficulty breathing. Allergic reactions are more common in individuals with existing allergies to other plants in the Allium genus. It's important to note that adverse reactions to garlic are not typically associated specifically with allicin but rather with the consumption or application of garlic itself. As with any supplement or natural remedy, it's essential to use garlic products cautiously and consult a healthcare professional, especially if you have underlying health conditions, allergies, or are taking medication.[17]
Dermatologic applications of Topical Garlic
Fungal infection
According to a study diallyl sulphide (DAS) and diallyl disulphide (DADS) significantly inhibit proteinase, phospholipase secretion and dimorphism in candida albicans. These compounds can, therefore, act as a potent anti-fungal in the management of candidiasis.
Additionally, ajoene, derived from garlic, has shown promising results in treating athlete's foot when formulated into a cream, offering a cost-effective and accessible option for managing superficial fungal infections, especially in resource-limited healthcare settings. These compounds have been shown to inhibit the growth of various fungal species, including Candida albicans and dermatophytes responsible for skin infections like athlete's foot and ringworm.[9-10]

Antioxidant effect[11]
The antioxidant effects of aged garlic extract, attributed to compounds like S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC), offer significant cellular protection by neutralizing reactive oxygen species (ROS), thereby mitigating oxidative damage and its associated aging and disease processes. Furthermore, aged garlic extract enhances the activity of crucial antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, bolstering the cell's defense mechanisms against oxidative stress. Additionally, the extract elevates intracellular levels of glutathione, a potent antioxidant molecule, providing an extra shield against oxidative injury.

UVB protection
Garlic boosts the growth of certain immune cells like macrophages and lymphocytes while also shielding against the weakening of the immune system caused by UV radiation. The components found in aged garlic extract shield against the UVB-induced reduction of contact hypersensitivity. This protection appears to occur by countering the effects of cis-uropionic acid, which mediates this type of immune suppression.[12]

Wound healing [13-14]
Research conducted by Bojs et al. highlights that allergic reactions to garlic might have a positive impact on wound healing. Furthermore, studies on chicken skin wounds treated with aged garlic extract revealed enhanced re-epithelialization and increased neovascularization in a dose-dependent manner, suggesting potential wound healing benefits. Additionally, garlic components have demonstrated antiviral properties, inhibiting the proliferation of virally infected cells. For instance, a placebo-controlled trial observed complete resolution of cutaneous warts without recurrence following the application of chloroform extracts of garlic over a period of 3–4 months. These findings underscore the multifaceted therapeutic potential of garlic in dermatology, ranging from wound healing to combating viral infections and skin conditions like warts.

Anti-aging
Garlic exhibits significant advantages for the sustained growth potential of fibroblasts, which are essential for preserving skin elasticity and integrity. This discovery suggests that garlic could be a promising anti-senescence and revitalizing agent. By augmenting the proliferative capacity of fibroblasts over a prolonged duration, garlic may bolster skin health and vibrancy, fostering a more youthful look and enhancing skin...
texture. Therefore, integrating garlic into skincare regimens or dietary habits may present a natural and efficacious strategy for addressing aging indicators and fostering comprehensive skin rejuvenation.[15]

Viral infection
Topical garlic has emerged as a potential treatment option for managing viral skin infections, owing to its reported antiviral properties. Garlic contains bioactive compounds such as allicin and ajoene, which have demonstrated direct antiviral activity against various viruses in laboratory studies. These compounds may disrupt viral replication processes, inhibit viral attachment to host cells, or interfere with viral protein synthesis, ultimately impeding viral infection and replication. Additionally, garlic extracts have been shown to modulate the immune response by stimulating immune cells such as macrophages and lymphocytes, enhancing the body's ability to combat viral infections. Furthermore, garlic's ability to counteract UV-induced immune suppression suggests a potential role in reducing the risk of viral skin infections triggered by UV radiation exposure. Clinical studies have reported positive outcomes with the use of garlic extracts in treating viral skin conditions such as cutaneous warts, highlighting its therapeutic potential in real-world settings. However, further research, including well-designed clinical trials, is needed to fully elucidate garlic's efficacy, safety, and optimal formulations for managing viral skin infections.[16]

Conclusion
The rise in fungal infections within hospital environments underscores the urgent need for effective interventions. Understanding the epidemiological landscape and the role of factors such as immunosuppression, medical advancements, and antimicrobial resistance is crucial for combating hospital-acquired infections (HAIs). Fungal diseases, particularly those caused by Candida species, pose significant challenges due to their opportunistic nature and ability to manifest in various anatomical sites. Garlic (Allium sativum) emerges as a promising natural remedy with broad-spectrum antimicrobial properties, including activity against fungi like Candida. Its diverse biochemical composition, encompassing sulfur compounds, enzymes, carbohydrates, minerals, amino acids, flavonoids, sapogenins, saponins, vitamins, and other constituents, contributes to its therapeutic effects. Notably, the synthesis of allicin, a key bioactive compound in garlic, highlights its role in antimicrobial action, including inhibition of fungal growth. Furthermore, dermatological applications of garlic offer potential solutions for fungal skin infections, wound healing, antioxidant protection, UVB shielding, and anti-aging benefits. Clinical evidence supports the efficacy of garlic extracts in managing viral skin conditions, suggesting a broader scope for its use in dermatology. The multifaceted therapeutic potential of garlic, coupled with its historical significance and widespread availability, positions it as a valuable asset in modern healthcare. Further research and clinical trials are warranted to fully explore its efficacy, safety, and optimal formulations, paving the way for enhanced patient outcomes and improved management of infectious diseases.

Acknowledgment
The authors express their gratitude to the Institute of Pharmaceutical Science and Research, Balaghat, for providing the necessary facilities to conduct this research. Special thanks are extended to Dr. Rajesh Mujariya for his invaluable support and guidance throughout the study.
There is no outsource funding from any institution, NGOs, personnel.

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